SEQUENCE LISTING

Zankel et al.

<120> USE OF THE CHAPERONE RECEPTOR-ASSOCIATED PROTEIN (RAP) FOR THE DELIVERY OF THERAPEUTIC COMPOUNDS TO THE BRAIN AND OTHER TISSUES

<130> 30610/39383

<140> US 10/600,862
<141> 2003-06-20

<160> 28

<170> PatentIn version 3.2

<210> 1
<211> 323
<212> PRT
<213> Homo sapiens

<400> 1

Tyr Ser Arg Glu Lys Asn Gln Pro Lys Pro Ser Pro Lys Arg Glu Ser
1 5 10 15

Gly Glu Glu Phe Arg Met Glu Lys Leu Asn Gln Leu Trp Glu Lys Ala
20 25 30

Gln Arg Leu His Leu Pro Pro Val Arg Leu Ala Glu Leu His Ala Asp
35 40 45

Leu Lys Ile Gln Glu Arg Asp Glu Leu Ala Trp Lys Lys Leu Lys Leu
50 55 60

Asp Gly Leu Asp Glu Asp Gly Glu Lys Glu Ala Arg Leu Ile Arg Asn
65 70 75 80

Leu Asn Val Ile Leu Ala Lys Tyr Gly Leu Asp Gly Lys Lys Asp Ala
85 90 95

Arg Gln Val Thr Ser Asn Ser Leu Ser Gly Thr Gln Glu Asp Gly Leu
100 105 110

Asp Asp Pro Arg Leu Glu Lys Leu Trp His Lys Ala Lys Thr Ser Gly
115 120 125

Lys Phe Ser Gly Glu Glu Leu Asp Lys Leu Trp Arg Glu Phe Leu His
130 135 140

His Lys Glu Lys Val His Glu Tyr Asn Val Leu Leu Glu Thr Leu Ser
145 150 155 160

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Arg Thr Glu Glu Ile His Glu Asn Val Ile Ser Pro Ser Asp Leu Ser
                165                 170                 175

Asp Ile Lys Gly Ser Val Leu His Ser Arg His Thr Glu Leu Lys Glu
            180                 185                 190

Lys Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu Arg Arg Val Ser
        195                 200                 205

His Gln Gly Tyr Ser Thr Glu Ala Glu Phe Glu Glu Pro Arg Val Ile
    210                 215                 220

Asp Leu Trp Asp Leu Ala Gln Ser Ala Asn Leu Thr Asp Lys Glu Leu
225                 230                 235                 240

Glu Ala Phe Arg Glu Glu Leu Lys His Phe Glu Ala Lys Ile Glu Lys
                245                 250                 255

His Asn His Tyr Gln Lys Gln Leu Glu Ile Ala His Glu Lys Leu Arg
            260                 265                 270

His Ala Glu Ser Val Gly Asp Gly Glu Arg Val Ser Arg Ser Arg Glu
        275                 280                 285

Lys His Ala Leu Leu Glu Gly Arg Thr Lys Glu Leu Gly Tyr Thr Val
    290                 295                 300

Lys Lys His Leu Gln Asp Leu Ser Gly Arg Ile Ser Arg Ala Arg His
305                 310                 315                 320

Ans Glu Leu
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<210> 2
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<213> Homo sapiens

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Pro Arg Leu Glu Lys Leu Trp His Lys Ala Lys Thr Ser Gly Lys Phe
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Ser Gly Glu Glu Leu Asp Lys Leu Trp Arg Glu Phe Leu His His Lys
            20                  25                  30

Glu Lys Val His Glu Tyr Asn Val Leu Leu Glu Thr Leu Ser Arg Thr
        35                  40                  45

Glu Glu Ile His Glu Asn Val Ile Ser Pro Ser Asp Leu Ser Asp Ile
    50                  55                  60
```

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Lys Gly Ser Val Leu His Ser Arg His Thr Glu Leu Lys Glu Lys Leu
65                  70                  75                  80

Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu Arg Arg Val Ser His Gln
                85                  90                  95

Gly Tyr Ser Thr Glu Ala Glu Phe Glu Glu Pro Arg Val Ile Asp Leu
            100                 105                 110

Trp Asp Leu Ala Gln Ser Ala Asn Leu Thr Asp Lys Glu Leu Glu Ala
        115                 120                 125

Phe Arg Glu Glu Leu Lys His Phe Glu Ala Lys Ile Glu Lys His Asn
    130                 135                 140

His Tyr Gln Lys Gln Leu Glu Ile Ala His Glu Lys Leu Arg His Ala
145                 150                 155                 160

Glu Ser Val Gly Asp Gly Glu Arg Val Ser Arg Ser Arg Glu Lys His
                165                 170                 175

Ala Leu Leu Glu Gly Arg Thr Lys Glu Leu Gly Tyr Thr Val Lys Lys
            180                 185                 190

His Leu Gln Asp Leu Ser Gly Arg Ile Ser Arg Ala Arg His Asn Glu
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Leu
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<210> 3
<211> 33
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic primer

<400> 3
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<210> 4
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<212> DNA
<213> Artificial sequence

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<223> Synthetic primer

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<211> 205
<212> PRT
<213> Homo sapiens

<400> 5

Pro Arg Leu Glu Lys Leu Trp His Lys Ala Lys Thr Ser Gly Ile Ser
1 5 10 15

Val Arg Leu Thr Ser Cys Ala Arg Val Leu His Tyr Lys Glu Lys Ile
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His Glu Tyr Asn Val Leu Leu Asp Thr Leu Ser Arg Ala Glu Glu Gly
35 40 45

Tyr Glu Asn Leu Leu Ser Pro Ser Asp Met Thr His Ile Lys Ser Asp
50 55 60

Thr Leu Ala Ser Lys His Ser Glu Leu Lys Asp Arg Leu Arg Ser Ile
65 70 75 80

Asn Gln Gly Leu Asp Arg Leu Arg Lys Val Ser His Gln Leu Arg Pro
85 90 95

Ala Thr Glu Phe Glu Glu Pro Arg Val Ile Asp Leu Trp Asp Leu Ala
100 105 110

Gln Ser Ala Asn Phe Thr Glu Lys Glu Leu Glu Ser Phe Arg Glu Glu
115 120 125

Leu Lys His Phe Glu Ala Lys Ile Glu Lys His Asn His Tyr Gln Lys
130 135 140

Gln Leu Glu Ile Ser His Gln Lys Leu Lys His Val Glu Ser Ile Gly
145 150 155 160

Asp Pro Glu His Ile Ser Arg Asn Lys Glu Lys Tyr Val Leu Leu Glu
165 170 175

Glu Lys Thr Lys Glu Leu Gly Tyr Lys Val Lys Lys His Leu Gln Asp
180 185 190

Leu Ser Ser Arg Val Ser Arg Ala Arg His Asn Glu Leu
195 200 205

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<211> 3702
<212> DNA

<213> Artificial sequence

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<223> RAP-GAA fusion sequence

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gaaaagctgt ggcacaaggc gaagacctct gggaaattct ccggcgaaga actggacaag 480

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ggcgacggcg agcgtgtgag ccgcagccgc gagaagcacg ccctgctgga ggggcggacc 960

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<211> 1228
<212> PRT
<213> Artificial sequence

<220>
<223> RAP-GAA fusion sequence

<400> 7

Met Arg Gly Pro Ser Gly Ala Leu Trp Leu Leu Leu Ala Leu Arg Thr
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Val Leu Gly Ser Tyr Ser Arg Glu Lys Asn Gln Pro Lys Pro Ser Pro
20 25 30

Lys Arg Glu Ser Gly Glu Glu Phe Arg Met Glu Lys Leu Asn Gln Leu
35 40 45

Trp Glu Lys Ala Gln Arg Leu His Leu Pro Pro Val Arg Leu Ala Glu
50 55 60

Leu His Ala Asp Leu Lys Ile Gln Glu Arg Asp Glu Leu Ala Trp Lys
65 70 75 80

Lys Leu Lys Leu Asp Gly Leu Asp Glu Asp Gly Glu Lys Glu Ala Arg
85 90 95

Leu Ile Arg Asn Leu Asn Val Ile Leu Ala Lys Tyr Gly Leu Asp Gly
100 105 110

Lys Lys Asp Ala Arg Gln Val Thr Ser Asn Ser Leu Ser Gly Thr Gln
115 120 125

Glu Asp Gly Leu Asp Asp Pro Arg Leu Glu Lys Leu Trp His Lys Ala
130 135 140

Lys Thr Ser Gly Lys Phe Ser Gly Glu Glu Leu Asp Lys Leu Trp Arg
145 150 155 160

Glu Phe Leu His His Lys Glu Lys Val His Glu Tyr Asn Val Leu Leu
165 170 175

Glu Thr Leu Ser Arg Thr Glu Glu Ile His Glu Asn Val Ile Ser Pro
180 185 190

Ser Asp Leu Ser Asp Ile Lys Gly Ser Val Leu His Ser Arg His Thr
195 200 205

```
Glu Leu Lys Glu Lys Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu
    210                 215                 220

Arg Arg Val Ser His Gln Gly Tyr Ser Thr Glu Ala Glu Phe Glu Glu
225                 230                 235                 240

Pro Arg Val Ile Asp Leu Trp Asp Leu Ala Gln Ser Ala Asn Leu Thr
                245                 250                 255

Asp Lys Glu Leu Glu Ala Phe Arg Glu Glu Leu Lys His Phe Glu Ala
            260                 265                 270

Lys Ile Glu Lys His Asn His Tyr Gln Lys Gln Leu Glu Ile Ala His
        275                 280                 285

Glu Lys Leu Arg His Ala Glu Ser Val Gly Asp Gly Glu Arg Val Ser
    290                 295                 300

Arg Ser Arg Glu Lys His Ala Leu Leu Glu Gly Arg Thr Lys Glu Leu
305                 310                 315                 320

Gly Tyr Thr Val Lys Lys His Leu Gln Asp Leu Ser Gly Arg Ile Ser
                325                 330                 335

Arg Ala Arg Ala Glu Ala Glu Thr Gly Ala His Pro Gly Arg Pro Arg
            340                 345                 350

Ala Val Pro Thr Gln Cys Asp Val Pro Pro Asn Ser Arg Phe Asp Cys
        355                 360                 365

Ala Pro Asp Lys Ala Ile Thr Gln Glu Gln Cys Glu Ala Arg Gly Cys
    370                 375                 380

Cys Tyr Ile Pro Ala Lys Gln Gly Leu Gln Gly Ala Gln Met Gly Gln
385                 390                 395                 400

Pro Trp Cys Phe Phe Pro Pro Ser Tyr Pro Ser Tyr Lys Leu Glu Asn
                405                 410                 415

Leu Ser Ser Ser Glu Met Gly Tyr Thr Ala Thr Leu Thr Arg Thr Thr
            420                 425                 430

Pro Thr Phe Phe Pro Lys Asp Ile Leu Thr Leu Arg Leu Asp Val Met
        435                 440                 445

Met Glu Thr Glu Asn Arg Leu His Phe Thr Ile Lys Asp Pro Ala Asn
    450                 455                 460
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Arg Arg Tyr Glu Val Pro Leu Glu Thr Pro Arg Val His Ser Arg Ala
465                 470                 475                 480

Pro Ser Pro Leu Tyr Ser Val Glu Phe Ser Glu Glu Pro Phe Gly Val
                485                 490                 495

Ile Val His Arg Gln Leu Asp Gly Arg Val Leu Leu Asn Thr Thr Val
            500                 505                 510

Ala Pro Leu Phe Phe Ala Asp Gln Phe Leu Gln Leu Ser Thr Ser Leu
        515                 520                 525

Pro Ser Gln Tyr Ile Thr Gly Leu Ala Glu His Leu Ser Pro Leu Met
    530                 535                 540

Leu Ser Thr Ser Trp Thr Arg Ile Thr Leu Trp Asn Arg Asp Leu Ala
545                 550                 555                 560

Pro Thr Pro Gly Ala Asn Leu Tyr Gly Ser His Pro Phe Tyr Leu Ala
                565                 570                 575

Leu Glu Asp Gly Gly Ser Ala His Gly Val Phe Leu Leu Asn Ser Asn
            580                 585                 590

Ala Met Asp Val Val Leu Gln Pro Ser Pro Ala Leu Ser Trp Arg Ser
        595                 600                 605

Thr Gly Gly Ile Leu Asp Val Tyr Ile Phe Leu Gly Pro Glu Pro Lys
    610                 615                 620

Ser Val Val Gln Gln Tyr Leu Asp Val Val Gly Tyr Pro Phe Met Pro
625                 630                 635                 640

Pro Tyr Trp Gly Leu Gly Phe His Leu Cys Arg Trp Gly Tyr Ser Ser
                645                 650                 655

Thr Ala Ile Thr Arg Gln Val Val Glu Asn Met Thr Arg Ala His Phe
            660                 665                 670

Pro Leu Asp Val Gln Trp Asn Asp Leu Asp Tyr Met Asp Ser Arg Arg
        675                 680                 685

Asp Phe Thr Phe Asn Lys Asp Gly Phe Arg Asp Phe Pro Ala Met Val
    690                 695                 700

Gln Glu Leu His Gln Gly Gly Arg Arg Tyr Met Met Ile Val Asp Pro
705                 710                 715                 720
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```
Ala Ile Ser Ser Ser Gly Pro Ala Gly Ser Tyr Arg Pro Tyr Asp Glu
                725                 730                 735

Gly Leu Arg Arg Gly Val Phe Ile Thr Asn Glu Thr Gly Gln Pro Leu
            740                 745                 750

Ile Gly Lys Val Trp Pro Gly Ser Thr Ala Phe Pro Asp Phe Thr Asn
        755                 760                 765

Pro Thr Ala Leu Ala Trp Trp Glu Asp Met Val Ala Glu Phe His Asp
    770                 775                 780

Gln Val Pro Phe Asp Gly Leu Trp Ile Asp Met Asn Glu Pro Ser Asn
785                 790                 795                 800

Phe Ile Arg Gly Ser Glu Asp Gly Cys Pro Asn Asn Glu Leu Glu Asn
                805                 810                 815

Pro Pro Tyr Val Pro Gly Val Val Gly Gly Thr Leu Gln Ala Ala Thr
            820                 825                 830

Ile Cys Ala Ser Ser His Gln Phe Leu Ser Thr His Tyr Asn Leu His
        835                 840                 845

Asn Leu Tyr Gly Leu Thr Glu Ala Ile Ala Ser His Arg Ala Leu Val
    850                 855                 860

Lys Ala Arg Gly Thr Arg Pro Phe Val Ile Ser Arg Ser Thr Phe Ala
865                 870                 875                 880

Gly His Gly Arg Tyr Ala Gly His Trp Thr Gly Asp Val Trp Ser Ser
                885                 890                 895

Trp Glu Gln Leu Ala Ser Ser Val Pro Glu Ile Leu Gln Phe Asn Leu
            900                 905                 910

Leu Gly Val Pro Leu Val Gly Ala Asp Val Cys Gly Phe Leu Gly Asn
        915                 920                 925

Thr Ser Glu Glu Leu Cys Val Arg Trp Thr Gln Leu Gly Ala Phe Tyr
    930                 935                 940

Pro Phe Met Arg Asn His Asn Ser Leu Leu Ser Leu Pro Gln Glu Pro
945                 950                 955                 960

Tyr Ser Phe Ser Glu Pro Ala Gln Gln Ala Met Arg Lys Ala Leu Thr
                965                 970                 975
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Leu Arg Tyr Ala Leu Leu Pro His Leu Tyr Thr Leu Phe His Gln Ala
            980                 985                 990

His Val Ala Gly Glu Thr Val Ala  Arg Pro Leu Phe Leu  Glu Phe Pro
        995                 1000                1005

Lys Asp  Ser Ser Thr Trp Thr  Val Asp His Gln Leu  Leu Trp Gly
    1010                1015                1020

Glu Ala  Leu Leu Ile Thr Pro  Val Leu Gln Ala Gly  Lys Ala Glu
    1025                1030                1035

Val Thr  Gly Tyr Phe Pro Leu  Gly Thr Trp Tyr Asp  Leu Gln Thr
    1040                1045                1050

Val Pro  Ile Glu Ala Leu Gly  Ser Leu Pro Pro Pro  Pro Ala Ala
    1055                1060                1065

Pro Arg  Glu Pro Ala Ile His  Ser Glu Gly Gln Trp  Val Thr Leu
    1070                1075                1080

Pro Ala  Pro Leu Asp Thr Ile  Asn Val His Leu Arg  Ala Gly Tyr
    1085                1090                1095

Ile Ile  Pro Leu Gln Gly Pro  Gly Leu Thr Thr Thr  Glu Ser Arg
    1100                1105                1110

Gln Gln  Pro Met Ala Leu Ala  Val Ala Leu Thr Lys  Gly Gly Glu
    1115                1120                1125

Ala Arg  Gly Glu Leu Phe Trp  Asp Asp Gly Glu Ser  Leu Glu Val
    1130                1135                1140

Leu Glu  Arg Gly Ala Tyr Thr  Gln Val Ile Phe Leu  Ala Arg Asn
    1145                1150                1155

Asn Thr  Ile Val Asn Glu Leu  Val Arg Val Thr Ser  Glu Gly Ala
    1160                1165                1170

Gly Leu  Gln Leu Gln Lys Val  Thr Val Leu Gly Val  Ala Thr Ala
    1175                1180                1185

Pro Gln  Gln Val Leu Ser Asn  Gly Val Pro Val Ser  Asn Phe Thr
    1190                1195                1200

Tyr Ser  Pro Asp Thr Lys Val  Leu Asp Ile Cys Val  Ser Leu Leu
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Met Gly Glu Gln Phe Leu Val Ser Trp Cys
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<210> 8
<211> 2937
<212> DNA
<213> Artificial sequence

<220>
<223> RAP-IDU fusion sequence

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gtgcacgtgt gtgcgcgccc cgagaagccg cccgggcagg tcacgcggct ccgcgccctg 2640

cccctgaccc aagggcagct ggttctggtc tggtcggatg aacacgtggg ctccaagtgc 2700

ctgtggacat acgagatcca gttctctcag gacggtaagg cgtacacccc ggtcagcagg 2760

aagccatcga ccttcaacct ctttgtgttc agcccagaca caggtgctgt ctctggctcc 2820

taccgagttc gagccctgga ctactgggcc cgaccaggcc ccttctcgga ccctgtgccg 2880

tacctggagg tccctgtgcc aagagggccc ccatccccgg gcaatccatg actcgag 2937

<210> 9
<211> 972
<212> PRT
<213> Artificial sequence

<220>
<223> RAP-IDU fusion sequence

<400> 9

Met Arg Gly Pro Ser Gly Ala Leu Trp Leu Leu Leu Ala Leu Arg Thr
1 5 10 15

Val Leu Gly Ser Tyr Ser Arg Glu Lys Asn Gln Pro Lys Pro Ser Pro
20 25 30

Lys Arg Glu Ser Gly Glu Glu Phe Arg Met Glu Lys Leu Asn Gln Leu
35 40 45

Trp Glu Lys Ala Gln Arg Leu His Leu Pro Pro Val Arg Leu Ala Glu
50 55 60

Leu His Ala Asp Leu Lys Ile Gln Glu Arg Asp Glu Leu Ala Trp Lys
65 70 75 80

Lys Leu Lys Leu Asp Gly Leu Asp Glu Asp Gly Glu Lys Glu Ala Arg
85 90 95

Leu Ile Arg Asn Leu Asn Val Ile Leu Ala Lys Tyr Gly Leu Asp Gly
100 105 110

Lys Lys Asp Ala Arg Gln Val Thr Ser Asn Ser Leu Ser Gly Thr Gln
115 120 125

Glu Asp Gly Leu Asp Asp Pro Arg Leu Glu Lys Leu Trp His Lys Ala
130 135 140

Lys Thr Ser Gly Lys Phe Ser Gly Glu Glu Leu Asp Lys Leu Trp Arg
145 150 155 160

Glu Phe Leu His His Lys Glu Lys Val His Glu Tyr Asn Val Leu Leu
165 170 175

Glu Thr Leu Ser Arg Thr Glu Glu Ile His Glu Asn Val Ile Ser Pro
180 185 190

Ser Asp Leu Ser Asp Ile Lys Gly Ser Val Leu His Ser Arg His Thr
195 200 205

Glu Leu Lys Glu Lys Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu
210 215 220

Arg Arg Val Ser His Gln Gly Tyr Ser Thr Glu Ala Glu Phe Glu Glu
225 230 235 240

Pro Arg Val Ile Asp Leu Trp Asp Leu Ala Gln Ser Ala Asn Leu Thr
245 250 255

Asp Lys Glu Leu Glu Ala Phe Arg Glu Glu Leu Lys His Phe Glu Ala
260 265 270

```
Lys Ile Glu Lys His Asn His Tyr Gln Lys Gln Leu Glu Ile Ala His
        275                 280                 285

Glu Lys Leu Arg His Ala Glu Ser Val Gly Asp Gly Glu Arg Val Ser
    290                 295                 300

Arg Ser Arg Glu Lys His Ala Leu Leu Glu Gly Arg Thr Lys Glu Leu
305                 310                 315                 320

Gly Tyr Thr Val Lys Lys His Leu Gln Asp Leu Ser Gly Arg Ile Ser
                325                 330                 335

Arg Ala Arg Ala Glu Ala Glu Thr Gly Glu Ala Pro His Leu Val His
            340                 345                 350

Val Asp Ala Ala Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg Ser
        355                 360                 365

Thr Gly Phe Cys Pro Pro Leu Pro His Ser Gln Ala Asp Gln Tyr Val
    370                 375                 380

Leu Ser Trp Asp Gln Gln Leu Asn Leu Ala Tyr Val Gly Ala Val Pro
385                 390                 395                 400

His Arg Gly Ile Lys Gln Val Arg Thr His Trp Leu Leu Glu Leu Val
                405                 410                 415

Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr Asn Phe Thr His
            420                 425                 430

Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu Asn Gln Leu Leu Pro Gly
        435                 440                 445

Phe Glu Leu Met Gly Ser Ala Ser Gly His Phe Thr Asp Phe Glu Asp
    450                 455                 460

Lys Gln Gln Val Phe Glu Trp Lys Asp Leu Val Ser Ser Leu Ala Arg
465                 470                 475                 480

Arg Tyr Ile Gly Arg Tyr Gly Leu Ala His Val Ser Lys Trp Asn Phe
                485                 490                 495

Glu Thr Trp Asn Glu Pro Asp His His Asp Phe Asp Asn Val Ser Met
            500                 505                 510

Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp Ala Cys Ser Glu Gly Leu
        515                 520                 525
```

```
Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly Gly Pro Gly Asp Ser Phe
    530                 535                 540

His Thr Pro Pro Arg Ser Pro Leu Ser Trp Gly Leu Leu Arg His Cys
545                 550                 555                 560

His Asp Gly Thr Asn Phe Phe Thr Gly Glu Ala Gly Val Arg Leu Asp
                565                 570                 575

Tyr Ile Ser Leu His Arg Lys Gly Ala Arg Ser Ser Ile Ser Ile Leu
            580                 585                 590

Glu Gln Glu Lys Val Val Ala Gln Gln Ile Arg Gln Leu Phe Pro Lys
        595                 600                 605

Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu Ala Asp Pro Leu Val Gly
    610                 615                 620

Trp Ser Leu Pro Gln Pro Trp Arg Ala Asp Val Thr Tyr Ala Ala Met
625                 630                 635                 640

Val Val Lys Val Ile Ala Gln His Gln Asn Leu Leu Leu Ala Asn Thr
                645                 650                 655

Thr Ser Ala Phe Pro Tyr Ala Leu Leu Ser Asn Asp Asn Ala Phe Leu
            660                 665                 670

Ser Tyr His Pro His Pro Phe Ala Gln Arg Thr Leu Thr Ala Arg Phe
        675                 680                 685

Gln Val Asn Asn Thr Arg Pro Pro His Val Gln Leu Leu Arg Lys Pro
    690                 695                 700

Val Leu Thr Ala Met Gly Leu Leu Ala Leu Leu Asp Glu Glu Gln Leu
705                 710                 715                 720

Trp Ala Glu Val Ser Gln Ala Gly Thr Val Leu Asp Ser Asn His Thr
                725                 730                 735

Val Gly Val Leu Ala Ser Ala His Arg Pro Gln Gly Pro Ala Asp Ala
            740                 745                 750

Trp Arg Ala Ala Val Leu Ile Tyr Ala Ser Asp Asp Thr Arg Ala His
        755                 760                 765

Pro Asn Arg Ser Val Ala Val Thr Leu Arg Leu Arg Gly Val Pro Pro
    770                 775                 780
```

```
Gly Pro Gly Leu Val Tyr Val Thr Arg Tyr Leu Asp Asn Gly Leu Cys
785                 790                 795                 800

Ser Pro Asp Gly Glu Trp Arg Arg Leu Gly Arg Pro Val Phe Pro Thr
                805                 810                 815

Ala Glu Gln Phe Arg Arg Met Arg Ala Ala Glu Asp Pro Val Ala Ala
            820                 825                 830

Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg Leu Thr Leu Arg Pro Ala
        835                 840                 845

Leu Arg Leu Pro Ser Leu Leu Leu Val His Val Cys Ala Arg Pro Glu
    850                 855                 860

Lys Pro Pro Gly Gln Val Thr Arg Leu Arg Ala Leu Pro Leu Thr Gln
865                 870                 875                 880

Gly Gln Leu Val Leu Val Trp Ser Asp Glu His Val Gly Ser Lys Cys
                885                 890                 895

Leu Trp Thr Tyr Glu Ile Gln Phe Ser Gln Asp Gly Lys Ala Tyr Thr
            900                 905                 910

Pro Val Ser Arg Lys Pro Ser Thr Phe Asn Leu Phe Val Phe Ser Pro
        915                 920                 925

Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg Val Arg Ala Leu Asp Tyr
    930                 935                 940

Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro Val Pro Tyr Leu Glu Val
945                 950                 955                 960

Pro Val Pro Arg Gly Pro Pro Ser Pro Gly Asn Pro
                965                 970
```

<210> 10
<211> 1398
<212> DNA
<213> Artificial sequence

<220>
<223> RAP-GDNF fusion sequence

<400> 10
atgggggttt cttactcgcg ggagaagaac cagcccaagc cgtccccgaa acgcgagtcc 60

ggagaggagt tccgcatgga gaagttgaac cagctgtggg agaaggccca gcgactgcat 120

cttcctcccg tgaggctggc cgagctccac gctgatctga agatacagga gagggacgaa 180

ctcgcctgga agaaactaaa gcttgacggc ttggacgaag atggggagaa ggaagcgaga 240

ctcatacgca acctcaatgt catcttggcc aagtatggtc tggacggaaa gaaggacgct 300

cggcaggtga ccagcaactc cctcagtggc acccaggaag acgggctgga tgaccccagg 360

ctggaaaagc tgtggcacaa ggcgaagacc tctgggaaat tctccggcga agaactggac 420

aagctctggc gggagttcct gcatcacaaa gagaaagttc acgagtacaa cgtcctgctg 480

gagaccctga gcaggaccga agaaatccac gagaacgtca ttagcccctc ggacctgagc 540

gacatcaagg gcagcgtcct gcacagcagg cacacggagc tgaaggagaa gctgcgcagc 600

atcaaccagg gcctggaccg cctgcgcagg gtcagccacc agggctacag cactgaggct 660

gagttcgagg agcccagggt gattgacctg tgggacctgg cgcagtccgc caacctcacg 720

gacaaggagc tggaggcgtt ccgggaggag ctcaagcact tcgaagccaa aatcgagaag 780

cacaaccact accagaagca gctggagatt gcgcacgaga agctgaggca cgcagagagc 840

gtgggcgacg gcgagcgtgt gagccgcagc cgcgagaagc acgccctgct ggaggggcgg 900

accaaggagc tgggctacac ggtgaagaag catctgcagg acctgtccgg caggatctcc 960

agagctcggg ccgaggcaga aaccggttca ccagataaac aaatggcagt gcttcctaga 1020

agagagcgga atcggcaggc tgcagctgcc aacccagaga attccagagg aaaaggtcgg 1080

agaggccaga ggggcaaaaa ccggggttgt gtcttaactg caatacattt aaatgtcact 1140

gacttgggtc tgggctatga aaccaaggag gaactgattt ttaggtactg cagcggctct 1200

tgcgatgcag ctgagacaac gtacgacaaa atattgaaaa acttatccag aaatagaagg 1260

ctggtgagtg acaaagtagg gcaggcatgt tgcagaccca tcgcctttga tgatgacctg 1320

tcgtttttag atgataacct ggtttaccat attctaagaa agcattccgc taaaaggtgt 1380

ggatgtatct gatctaga 1398

<210> 11
<211> 463
<212> PRT
<213> Artificial sequence

<220>
<223> RAP-GDNF fusion sequence

<400> 11

Met Gly Gly Ser Tyr Ser Arg Glu Lys Asn Gln Pro Lys Pro Ser Pro
1 5 10 15

Lys Arg Glu Ser Gly Glu Glu Phe Arg Met Glu Lys Leu Asn Gln Leu
20 25 30

Trp Glu Lys Ala Gln Arg Leu His Leu Pro Pro Val Arg Leu Ala Glu
35 40 45

```
Leu His Ala Asp Leu Lys Ile Gln Glu Arg Asp Glu Leu Ala Trp Lys
    50                  55                  60

Lys Leu Lys Leu Asp Gly Leu Asp Glu Asp Gly Glu Lys Glu Ala Arg
65                  70                  75                  80

Leu Ile Arg Asn Leu Asn Val Ile Leu Ala Lys Tyr Gly Leu Asp Gly
                85                  90                  95

Lys Lys Asp Ala Arg Gln Val Thr Ser Asn Ser Leu Ser Gly Thr Gln
            100                 105                 110

Glu Asp Gly Leu Asp Asp Pro Arg Leu Glu Lys Leu Trp His Lys Ala
        115                 120                 125

Lys Thr Ser Gly Lys Phe Ser Gly Glu Glu Leu Asp Lys Leu Trp Arg
    130                 135                 140

Glu Phe Leu His His Lys Glu Lys Val His Glu Tyr Asn Val Leu Leu
145                 150                 155                 160

Glu Thr Leu Ser Arg Thr Glu Glu Ile His Glu Asn Val Ile Ser Pro
                165                 170                 175

Ser Asp Leu Ser Asp Ile Lys Gly Ser Val Leu His Ser Arg His Thr
            180                 185                 190

Glu Leu Lys Glu Lys Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu
        195                 200                 205

Arg Arg Val Ser His Gln Gly Tyr Ser Thr Glu Ala Glu Phe Glu Glu
    210                 215                 220

Pro Arg Val Ile Asp Leu Trp Asp Leu Ala Gln Ser Ala Asn Leu Thr
225                 230                 235                 240

Asp Lys Glu Leu Glu Ala Phe Arg Glu Glu Leu Lys His Phe Glu Ala
                245                 250                 255

Lys Ile Glu Lys His Asn His Tyr Gln Lys Gln Leu Glu Ile Ala His
            260                 265                 270

Glu Lys Leu Arg His Ala Glu Ser Val Gly Asp Gly Glu Arg Val Ser
        275                 280                 285

Arg Ser Arg Glu Lys His Ala Leu Leu Glu Gly Arg Thr Lys Glu Leu
    290                 295                 300
```

```
Gly Tyr Thr Val Lys Lys His Leu Gln Asp Leu Ser Gly Arg Ile Ser
305                 310                 315                 320

Arg Ala Arg Ala Glu Ala Glu Thr Gly Ser Pro Asp Lys Gln Met Ala
                325                 330                 335

Val Leu Pro Arg Arg Glu Arg Asn Arg Gln Ala Ala Ala Ala Asn Pro
            340                 345                 350

Glu Asn Ser Arg Gly Lys Gly Arg Arg Gly Gln Arg Gly Lys Asn Arg
        355                 360                 365

Gly Cys Val Leu Thr Ala Ile His Leu Asn Val Thr Asp Leu Gly Leu
    370                 375                 380

Gly Tyr Glu Thr Lys Glu Glu Leu Ile Phe Arg Tyr Cys Ser Gly Ser
385                 390                 395                 400

Cys Asp Ala Ala Glu Thr Thr Tyr Asp Lys Ile Leu Lys Asn Leu Ser
                405                 410                 415

Arg Asn Arg Arg Leu Val Ser Asp Lys Val Gly Gln Ala Cys Cys Arg
            420                 425                 430

Pro Ile Ala Phe Asp Asp Asp Leu Ser Phe Leu Asp Asp Asn Leu Val
        435                 440                 445

Tyr His Ile Leu Arg Lys His Ser Ala Lys Arg Cys Gly Cys Ile
    450                 455                 460
```

<210> 12
<211> 49
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic primer

<400> 12
gcgataggat cctactcgcg ggagaagaac cagcccaagc cgtccccga 49

<210> 13
<211> 57
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic primer

<400> 13
gcgataaacc ggtttctgcc tcggcgcgag ctctggagat cctgccggac aggtcct 57

<210> 14
<211> 39
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic primer

<400> 14
gcgataaccg gtgcacaccc cggccgtccc agagcagtg 39

<210> 15
<211> 37
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic primer

<400> 15
gcgatactcg agtcaacacc agctgacgag aaactgc 37

<210> 16
<211> 46
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic primer

<400> 16
gcgataaccg gtgaggcccc ccgcacctgg tgcatgtgga cgcggc 46

<210> 17
<211> 45
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic primer

<400> 17
gcgatactcg agtcatggat tgcccgggga tgggggccct cttgg 45

<210> 18
<211> 33
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic primer

<400> 18
acagtgaccg gttcaccaga taaacaaatg gca 33

<210> 19
<211> 38

<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic primer

<400> 19
acagtgctcg agtctagatc agatacatcc acaccttt 38

<210> 20
<211> 51
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic primer

<400> 20
acagtggcca tgggggttc ttactcgcgg gagaagaacc agcccaagcc g 51

<210> 21
<211> 357
<212> PRT
<213> Homo sapiens

<400> 21

Met Ala Pro Arg Arg Val Arg Ser Phe Leu Arg Gly Leu Pro Ala Leu
1 5 10 15

Leu Leu Leu Leu Leu Phe Leu Gly Pro Trp Pro Ala Ala Ser His Gly
20 25 30

Gly Lys Tyr Ser Arg Glu Lys Asn Gln Pro Lys Pro Ser Pro Lys Arg
35 40 45

Glu Ser Gly Glu Glu Phe Arg Met Glu Lys Leu Asn Gln Leu Trp Glu
50 55 60

Lys Ala Gln Arg Leu His Leu Pro Pro Val Arg Leu Ala Glu Leu His
65 70 75 80

Ala Asp Leu Lys Ile Gln Glu Arg Asp Glu Leu Ala Trp Lys Lys Leu
85 90 95

Lys Leu Asp Gly Leu Asp Glu Asp Gly Glu Lys Glu Ala Arg Leu Ile
100 105 110

Arg Asn Leu Asn Val Ile Leu Ala Lys Tyr Gly Leu Asp Gly Lys Lys
115 120 125

Asp Ala Arg Gln Val Thr Ser Asn Ser Leu Ser Gly Thr Gln Glu Asp
130 135 140

```
Gly Leu Asp Asp Pro Arg Leu Glu Lys Leu Trp His Lys Ala Lys Thr
145                 150                 155                 160

Ser Gly Lys Phe Ser Gly Glu Glu Leu Asp Lys Leu Trp Arg Glu Phe
                165                 170                 175

Leu His His Lys Glu Lys Val His Glu Tyr Asn Val Leu Leu Glu Thr
            180                 185                 190

Leu Ser Arg Thr Glu Glu Ile His Glu Asn Val Ile Ser Pro Ser Asp
        195                 200                 205

Leu Ser Asp Ile Lys Gly Ser Val Leu His Ser Arg His Thr Glu Leu
    210                 215                 220

Lys Glu Lys Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu Arg Arg
225                 230                 235                 240

Val Ser His Gln Gly Tyr Ser Thr Glu Ala Glu Phe Glu Glu Pro Arg
                245                 250                 255

Val Ile Asp Leu Trp Asp Leu Ala Gln Ser Ala Asn Leu Thr Asp Lys
            260                 265                 270

Glu Leu Glu Ala Phe Arg Glu Glu Leu Lys His Phe Glu Ala Lys Ile
        275                 280                 285

Glu Lys His Asn His Tyr Gln Lys Gln Leu Glu Ile Ala His Glu Lys
    290                 295                 300

Leu Arg His Ala Glu Ser Val Gly Asp Gly Glu Arg Val Ser Arg Ser
305                 310                 315                 320

Arg Glu Lys His Ala Leu Leu Glu Gly Arg Thr Lys Glu Leu Gly Tyr
                325                 330                 335

Thr Val Lys Lys His Leu Gln Asp Leu Ser Gly Arg Ile Ser Arg Ala
            340                 345                 350

Arg His Asn Glu Leu
        355
```

<210> 22
<211> 378
<212> PRT
<213> Mus musculus

<400> 22

```
Met Gly Gly Pro Thr Arg Pro Ser Pro Val Ser Leu Leu Ala Leu Gln
1               5                  10                  15

Arg Lys Met Ala Pro Arg Arg Glu Arg Val Ser Thr Leu Pro Arg Leu
            20                  25                  30

Gln Leu Leu Val Leu Leu Leu Leu Pro Leu Met Leu Val Pro Gln Pro
        35                  40                  45

Ile Ala Gly His Gly Gly Lys Tyr Ser Arg Glu Lys Asn Glu Pro Glu
    50                  55                  60

Met Ala Ala Lys Arg Glu Ser Gly Glu Glu Phe Arg Met Glu Lys Leu
65                  70                  75                  80

Asn Gln Leu Trp Glu Lys Ala Lys Arg Leu His Leu Ser Pro Val Arg
                85                  90                  95

Leu Ala Glu Leu His Ser Asp Leu Lys Ile Gln Glu Arg Asp Glu Leu
            100                 105                 110

Asn Trp Lys Lys Leu Lys Val Glu Gly Leu Asp Lys Asp Gly Glu Lys
        115                 120                 125

Glu Ala Lys Leu Ile His Asn Leu Asn Val Ile Leu Ala Arg Tyr Gly
    130                 135                 140

Leu Asp Gly Arg Lys Asp Ala Gln Met Val His Ser Asn Ala Leu Asn
145                 150                 155                 160

Glu Asp Thr Gln Asp Glu Leu Gly Asp Pro Arg Leu Glu Lys Leu Trp
                165                 170                 175

His Lys Ala Lys Thr Ser Gly Lys Phe Ser Ser Glu Glu Leu Asp Lys
            180                 185                 190

Leu Trp Arg Glu Phe Leu His Tyr Lys Glu Lys Ile Gln Glu Tyr Asn
        195                 200                 205

Val Leu Leu Asp Thr Leu Ser Arg Ala Glu Glu Gly Tyr Glu Asn Leu
    210                 215                 220

Leu Ser Pro Ser Asp Met Ala His Ile Lys Ser Asp Thr Leu Ile Ser
225                 230                 235                 240

Lys His Ser Glu Leu Lys Asp Arg Leu Arg Ser Ile Asn Gln Gly Leu
                245                 250                 255
```

```
Asp Arg Leu Arg Lys Val Ser His Gln Gly Tyr Gly Ser Thr Thr Glu
            260                 265                 270

Phe Glu Glu Pro Arg Val Ile Asp Leu Trp Asp Leu Ala Gln Ser Ala
        275                 280                 285

Asn Phe Thr Glu Lys Glu Leu Glu Ser Phe Arg Glu Glu Leu Lys His
    290                 295                 300

Phe Glu Ala Lys Ile Glu Lys His Asn His Tyr Gln Lys Gln Leu Glu
305                 310                 315                 320

Ile Ser His Gln Lys Leu Lys His Val Glu Ser Ile Gly Asp Pro Glu
                325                 330                 335

His Ile Ser Arg Asn Lys Glu Lys Tyr Val Leu Leu Glu Glu Lys Thr
            340                 345                 350

Lys Glu Leu Gly Tyr Lys Val Lys Lys His Leu Gln Asp Leu Ser Ser
        355                 360                 365

Arg Val Ser Arg Ala Arg His Asn Glu Leu
    370                 375
```

<210> 23
<211> 357
<212> PRT
<213> Rat

<400> 23

```
Leu Arg Asp Arg Val Ser Thr Leu Pro Arg Leu Gln Leu Leu Val Leu
1               5                   10                  15

Leu Leu Leu Pro Leu Leu Leu Val Pro Gln Pro Ile Ala Gly His Gly
            20                  25                  30

Gly Lys Tyr Ser Arg Glu Lys Asn Glu Pro Glu Met Ala Ala Lys Arg
        35                  40                  45

Glu Ser Gly Glu Glu Phe Arg Met Glu Lys Leu Asn Gln Leu Trp Glu
    50                  55                  60

Lys Ala Lys Arg Leu His Leu Ser Pro Val Arg Leu Ala Glu Leu His
65                  70                  75                  80

Ser Asp Leu Lys Ile Gln Glu Arg Asp Glu Leu Asn Trp Lys Lys Leu
                85                  90                  95
```

```
Lys Val Glu Gly Leu Asp Gly Asp Gly Glu Lys Glu Ala Lys Leu Val
            100                 105                 110

His Asn Leu Asn Val Ile Leu Ala Arg Tyr Gly Leu Asp Gly Arg Lys
        115                 120                 125

Asp Thr Gln Thr Val His Ser Asn Ala Leu Asn Glu Asp Thr Gln Asp
    130                 135                 140

Glu Leu Gly Asp Pro Arg Leu Glu Lys Leu Trp His Lys Ala Lys Thr
145                 150                 155                 160

Ser Gly Lys Phe Ser Ser Glu Glu Leu Asp Lys Leu Trp Arg Glu Phe
                165                 170                 175

Leu His Tyr Lys Glu Lys Ile His Glu Tyr Asn Val Leu Leu Asp Thr
            180                 185                 190

Leu Ser Arg Ala Glu Glu Gly Tyr Glu Asn Leu Leu Ser Pro Ser Asp
        195                 200                 205

Met Thr His Ile Lys Ser Asp Thr Leu Ala Ser Lys His Ser Glu Leu
    210                 215                 220

Lys Asp Arg Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu Arg Lys
225                 230                 235                 240

Val Ser His Gln Gly Tyr Gly Pro Ala Thr Glu Phe Glu Glu Pro Arg
                245                 250                 255

Val Ile Asp Leu Trp Asp Leu Ala Gln Ser Ala Asn Phe Thr Glu Lys
            260                 265                 270

Glu Leu Glu Ser Phe Arg Glu Glu Leu Lys His Phe Glu Ala Lys Ile
        275                 280                 285

Glu Lys His Asn His Tyr Gln Lys Gln Leu Glu Ile Ser His Gln Lys
    290                 295                 300

Leu Lys His Val Glu Ser Ile Gly Asp Pro Glu His Ile Ser Arg Asn
305                 310                 315                 320

Lys Glu Lys Tyr Val Leu Leu Glu Glu Lys Thr Lys Glu Leu Gly Tyr
                325                 330                 335

Lys Val Lys Lys His Leu Gln Asp Leu Ser Ser Arg Val Ser Arg Ala
            340                 345                 350
```

Arg His Asn Glu Leu
355

<210> 24
<211> 348
<212> PRT
<213> Chicken

<400> 24

Met Gly Ala Thr Arg Thr Leu Val Ala Val Met Ala Ala Phe Leu Ala
1 5 10 15

Val Ser Thr Arg Ala Ser Lys Tyr Thr Arg Glu Ala Asn Glu Gly Leu
20 25 30

Ala Asp Ala Lys Arg Arg Glu Ala Gly Glu Phe Arg Val Val Arg Leu
35 40 45

Asn Gln Val Trp Glu Lys Ala Gln Arg Leu Gln Leu Ser Ala Val Lys
50 55 60

Leu Ala Glu Leu His Ser Asp Leu Lys Ile Gln Glu Lys Asp Glu Leu
65 70 75 80

Ser Trp Lys Lys Leu Lys Ala Glu Gly Leu Gly Glu Asp Gly Glu Lys
85 90 95

Glu Ala Lys Leu Arg Arg Asn Ile Asn Val Ile Met Thr Lys Tyr Gly
100 105 110

Met Asn Gly Lys Lys Asp Ser His Leu Thr Asp Thr Asn Tyr Ile Lys
115 120 125

Asp Gly Thr Glu Ser Asp Thr Leu Asp Asp Pro Arg Leu Glu Lys Leu
130 135 140

Trp Ser Lys Ala Lys Thr Ser Gly Lys Phe Ser Asp Glu Glu Leu Asp
145 150 155 160

Lys Leu Trp Arg Glu Phe Lys His His Lys Glu Lys Ile Arg Glu Tyr
165 170 175

Asn Ile Leu Leu Glu Thr Val Ser Arg Thr Glu Asp Ile His Lys Lys
180 185 190

Val Ile Asn Pro Ser Glu Glu Asn Pro Val Lys Glu Glu Val Leu His
195 200 205

```
Asn Lys His Arg Glu Leu Lys Glu Lys Leu Arg Ser Ile Asn Gln Gly
    210                 215                 220

Phe Glu Arg Leu Arg Lys Val Ser His Gln Gly Tyr Asp Ala Thr Ser
225                 230                 235                 240

Glu Phe Glu Glu Pro Arg Val Ile Asp Leu Trp Asp Met Ala Lys Ser
                245                 250                 255

Ala Asn Phe Thr Glu Lys Glu Leu Glu Ser Phe Arg Glu Glu Leu Lys
            260                 265                 270

His Phe Glu Ala Lys Ile Glu Lys His His His Tyr Gln Lys Gln Leu
        275                 280                 285

Glu Ile Ser His Glu Lys Leu Lys His Ile Glu Gly Thr Gly Asp Lys
    290                 295                 300

Glu His Leu Asn Arg Asn Arg Glu Lys Tyr Ala Met Leu Glu Glu Lys
305                 310                 315                 320

Thr Lys Glu Leu Gly Tyr Lys Val Lys Lys His Leu Gln Asp Leu Ser
                325                 330                 335

Ser Arg Ile Ser Gln Gly Leu Gln His Asn Glu Leu
            340                 345
```

<210> 25
<211> 331
<212> PRT
<213> Zebrafish

<400> 25

```
Met Ala Gly Lys Tyr Ser Lys Glu Met Asn Glu Lys Asn Ala Ser Asp
1               5                   10                  15

Lys Ser Asn Asn Gln Val Glu Phe Arg Ile Ala Lys Leu Asn Gln Val
            20                  25                  30

Trp Glu Lys Ala Ile Arg Met Gln Leu Ala Pro Val Arg Leu Ser Glu
        35                  40                  45

Leu His Ser Asp Leu Lys Ile Gln Glu Lys Asp Glu Leu Gln Trp Lys
    50                  55                  60

Lys Leu Lys Ala Glu Gly Met Asp Glu Asp Gly Glu Arg Glu Ala Lys
65                  70                  75                  80
```

```
Leu Arg Arg Asn Phe Asn Ile Ile Leu Ala Lys Tyr Gly Met Asp Gly
                85                  90                  95

Lys Lys Asp Thr Arg Thr Leu Asp Ser Asn Arg Leu Lys Asp His Glu
            100                 105                 110

Val Lys Ile Gly Asp Thr Phe Asp Asp Pro Lys Leu Asp Lys Leu Trp
        115                 120                 125

Asn Lys Ala Arg Thr Ser Gly Lys Phe Ser Asp Glu Glu Leu Gln Thr
    130                 135                 140

Leu His Arg Glu Phe Gln His His Lys Asp Lys Ile His Glu Tyr Asn
145                 150                 155                 160

Ile Val Met Asp Thr Val Ser Arg Thr Glu Glu Ile His Lys Asn Val
                165                 170                 175

Ile Ser Pro Leu Glu Gly Asp Val Lys Glu Asn Val Leu His Gln Lys
            180                 185                 190

His Thr Asp Leu Lys Gln Arg Met Arg Asp Leu Asn Gln Gly Phe Glu
        195                 200                 205

Arg Leu Arg Lys Ile Thr His Glu Gly Tyr Thr Asp Asp Ser Glu Phe
    210                 215                 220

Arg Glu Pro Arg Val Ile Glu Leu Trp Glu Met Ala Lys Arg Ser Asn
225                 230                 235                 240

Leu Ser Glu Asp Glu Leu Asp Ser Leu Lys Glu Glu Leu Arg His Phe
                245                 250                 255

Glu Thr Lys Val Glu Lys His Gln His Tyr Gln Glu Gln Leu Glu Leu
            260                 265                 270

Ser His Gln Lys Leu Lys His Val Glu Ala Leu Gly Asp Glu Asp His
        275                 280                 285

Ile Met Arg Asn Lys Glu Lys Tyr Asn Thr Leu Ala Glu Lys Ala Arg
    290                 295                 300

Glu Met Gly Tyr Lys Met Lys Lys His Leu Gln Asp Leu Thr Asn Lys
305                 310                 315                 320

Leu Ser Lys Asn Gly Leu Gln His Asn Glu Leu
                325                 330
```

<210> 26
<211> 379
<212> PRT
<213> Fruit fly

<400> 26

```
Met Val Arg Ser Ala Leu Val Val Ala Ala Ile Ala Leu Ser Val Leu
1               5                  10                  15

Ile Ala Leu Gln Gly Val Asp Ala Asp Lys Lys Gln Ser Lys Lys Tyr
            20                  25                  30

Ser Lys Glu Ala Asn Asp Pro His Phe Gln Gln Val Lys Gln Glu Lys
        35                  40                  45

Tyr Asp Pro Asp Phe Lys Ser Ile Gln Arg Pro Phe Arg Met Ala Lys
    50                  55                  60

Leu Asn Leu Val Trp Ala Lys Ala Gln Asn Arg Leu Thr Glu Pro Lys
65                  70                  75                  80

Leu Lys Ser Leu Tyr Met Glu Leu Lys Ile His Asp Lys Glu Glu Ile
                85                  90                  95

Ala Trp Lys Gln Leu Asn Ser Gln His Lys Asp Lys Asp Gly Leu Lys
            100                 105                 110

Ala Asp Glu Leu Arg Arg Lys Leu Ile Gly Ile Met Ser Ser Tyr Asp
        115                 120                 125

Leu Leu Glu His Phe Asp Asp Thr Gln Asp Thr Glu Lys Leu Lys Pro
    130                 135                 140

Tyr Lys Lys Phe His Asp Ala Glu Glu Arg His Arg Asn Lys Ser Leu
145                 150                 155                 160

Phe Lys Asp Lys Lys Leu Asn Arg Leu Trp Glu Lys Ala Glu Ile Ser
                165                 170                 175

Gly Phe Thr Ala Glu Glu Leu Lys Ser Leu Lys Gln Glu Phe Asp His
            180                 185                 190

His Gln Asp Lys Val Asp Val Tyr Tyr Ser Leu Leu Glu Asn Ile Gly
        195                 200                 205

Thr Val Asp Thr Asp Lys His Glu Asn Ala Ile Asn Thr Glu Asp Leu
    210                 215                 220
```

```
Asp Thr Tyr Asn Leu Ile Ser Asn Asp Val Asn Glu Asn Asp Ile Lys
225                 230                 235                 240

Thr His Ala Gln Asn Val Lys Ser Phe Glu Asn Asp Leu Asn Thr Leu
                245                 250                 255

Arg Gly His His Thr Gly Ile Lys Asp His Tyr Asp Arg Leu Glu Arg
            260                 265                 270

Leu Val Ser Ser Gly Pro His Ser Gln Asp Phe Ile Glu Pro Lys Val
        275                 280                 285

Gln Gly Leu Trp Arg Val Ala Gln Ala Ser Asn Phe Thr Val Lys Glu
    290                 295                 300

Leu Glu Ser Ile Lys Thr Glu Leu His His Phe Glu Ser Arg Leu Leu
305                 310                 315                 320

Lys Leu Arg His Leu His Ala Glu His Ala Leu Gln Lys Glu Lys Tyr
                325                 330                 335

Lys Gly Glu Lys Val Lys Asp Lys Ser Ser Arg Phe Glu Glu Met Glu
            340                 345                 350

Asp Gln Leu Lys Lys Gln Thr Arg Lys Val Glu Lys Leu Gln Glu Asn
        355                 360                 365

Ile Glu Lys Thr Ile Phe Lys His Thr Glu Leu
    370                 375
```

<210> 27
<211> 400
<212> PRT
<213> Mosquito

<400> 27

```
Glu Leu Cys Pro Ile Ala Arg Arg Lys Arg Gly Ile Lys His Thr Leu
1               5                   10                  15

Thr Met Pro Leu Phe Thr Arg Leu Cys Val Ile Val Phe Thr Val Leu
            20                  25                  30

Val Cys Asn His Val Val Gln Ser Glu Lys Ala His Ser Lys Tyr Ser
        35                  40                  45

Lys His Ala Asn Ala Leu Pro Asp Ser Glu Ile Tyr Glu Pro Asp Phe
    50                  55                  60
```

```
Arg Asn Ile Gln Arg Pro Phe Arg Met Ala Lys Leu Asn Leu Val Trp
65                  70                  75                  80

Thr Lys Ala Gln His Arg Leu Thr Glu Pro Lys Leu Lys Ser Leu Tyr
                85                  90                  95

Thr Glu Leu Lys Leu His Asp Lys Glu Glu Leu Thr Tyr Lys Gln Leu
            100                 105                 110

Lys Glu Lys Asp Lys Asp Gly Leu Lys Glu Ala Glu Leu Arg Asn Lys
        115                 120                 125

Leu Val Ser Ile Met Ser Thr Tyr Gly Leu Leu Glu His Phe Asp Asp
    130                 135                 140

Thr Gln Asp Pro Glu Lys Tyr Lys Leu Ala Lys Ser Ser Asp Gly Ala
145                 150                 155                 160

Pro Lys Lys Asp Thr Tyr Lys Asn Lys Ser Leu Phe Lys Asp Lys Lys
                165                 170                 175

Leu Asn Lys Leu Trp Asp Lys Ala Glu Ser Ala Gly Phe Thr Lys Glu
            180                 185                 190

Glu Leu Asp Ala Leu Arg Glu Glu Phe Asp His His Gln Ala Lys Ile
        195                 200                 205

Asp Val Tyr Tyr Ser Leu Leu Glu Arg Leu Gly Asp Asp Asp Asp Gly
    210                 215                 220

Gly Ala Ala Gly Gln Gly Ser Arg Arg Asp Asp Asp Ala Leu Leu Asn
225                 230                 235                 240

Ala Val Asn Asp Glu Glu His Asp Arg Tyr Asn Glu Val Asp Arg Ala
                245                 250                 255

Glu Glu Thr Asp Arg Ser Gln Pro Gly Ala Asn Lys Gln His Ala Tyr
            260                 265                 270

Leu His Lys Ser Asn Gln Leu Arg Glu Lys His Arg Glu Ile Arg Asp
        275                 280                 285

Asn Phe Asp Arg Leu Asp Arg Ile Ala Ser Lys Gly Pro Lys Ser Gln
    290                 295                 300

Asp Phe Val Glu Pro Lys Val Gln Gly Leu Trp Arg Val Ala Leu Ala
305                 310                 315                 320
```

Ser Asp Phe Ser Ala Asp Glu Leu Ala Ser Leu Lys Val Glu Leu Leu
325 330 335

His Tyr Glu Ser Arg Leu Leu Lys Leu Arg His Met His Ala Glu His
340 345 350

Ala Leu Ser Leu Glu Lys His Lys His Ser Asp Ala Lys Ala Asp Thr
355 360 365

His Lys Leu Met Glu Asp Asn Ile Lys Lys Gln Thr Arg Lys Val Glu
370 375 380

Lys Met Gln Glu Glu Val Glu Arg Arg Ile Phe Lys His Ser Glu Leu
385 390 395 400

<210> 28
<211> 331
<212> PRT
<213> Flatworm

<400> 28

Met Arg Asn His Phe Ser Phe Leu Leu Phe Leu Leu Val Ile Gly Ser
1 5 10 15

Ala His Asn Lys Lys Thr Gln Tyr Arg Thr Glu Arg Ile Asn Phe Ile
20 25 30

Tyr Glu Lys Ala Leu Gln His Val Thr Asp Arg Gln Asn Leu Ala Arg
35 40 45

Leu Glu Lys Glu Leu Ser Gly Tyr Asp Ala Ile Tyr Leu Ala Ser Lys
50 55 60

Ser Asn Arg Gln Gly Thr Gln Gly Thr Lys Glu Ile Asp Lys Ile Asp
65 70 75 80

Asp Lys Leu Gly Lys Ile Leu Glu Lys Tyr Gly Leu Glu Lys Ala Val
85 90 95

Leu Ala Phe Lys Glu Lys Tyr Lys His Lys Asn Leu Phe Gln Gln Thr
100 105 110

Asp Asp Asn Glu Pro Leu Pro Ser Gly Lys Phe Thr Asp Gln Asn Leu
115 120 125

Gln Lys Leu Trp Ser Gln Ala Gln Asn Gly Lys Phe Ser Gln Lys Glu
130 135 140

```
Leu Asn Ala Leu His Gly Glu Leu Lys Glu Val Glu Gln Lys Met Arg
145                 150                 155                 160

Val Tyr Glu Asp Gln Leu Asp Asp Phe Lys Lys Val Pro His Glu Asn
                165                 170                 175

Ser Ile Gln His Asp Ile Glu Ser Ile Gly Asp Lys Thr Lys Lys Leu
            180                 185                 190

Lys Ala Ala Asn Arg Glu Leu Asn Asp His Leu Asp Glu Val His Arg
        195                 200                 205

Lys Val Thr Ser Glu Glu Phe Ser Pro Phe Asn Glu Pro Arg Val Lys
    210                 215                 220

Arg Leu Trp Lys Leu Ala Gln Glu Asn Glu Lys Leu Thr Pro His Glu
225                 230                 235                 240

Leu Ser Val Leu Lys Asp Glu Leu Ser His Phe Glu Ser Gln Leu Lys
                245                 250                 255

Lys Ile Glu Phe His Lys Val Phe Phe Phe Val Ala Asn Ser Cys Pro
            260                 265                 270

Lys Arg Gly Lys Asn Glu Glu Val Ser Arg Leu Gln Glu Asp Ala Glu
        275                 280                 285

Glu Arg Gly Lys Asp Lys Ser Gln Val Tyr Glu Asn Leu Glu Leu Ser
    290                 295                 300

Ile Lys His Glu Lys Leu Asn Arg Lys Ala Arg Lys Leu Glu Lys Tyr
305                 310                 315                 320

Ile Glu Glu Lys Ile Ile Ile His Arg Glu Leu
                325                 330
```